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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/562,297 | 12/22/2005 | Christopher S. Burgey | 21382YP | 3740 |
| 210 | 7590 | 03/31/2008 | EXAMINER | |
| MERCK AND CO., INC | | | KIFLE, BRUCK | |
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

| | | | |
|------------------------------|--------------------------------------|--------------------------------------|--|
| Office Action Summary | Application No. 10/562,297 | Applicant(s) BURGEY ET AL. | |
| | Examiner Bruck Kifle | Art Unit 1624 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 February 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>12/22/05</u> . | 6) <input type="checkbox"/> Other: _____ |

Election/Restrictions

Applicant's election without traverse of group I in the reply filed on 02/19/08 is acknowledged.

Claim Rejections - 35 USC § 112

Claims 1-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) The term "heteroaryl" is indefinite because it is not known how many atoms are present, how many and what kind of heteroatoms are involved, what size ring is intended and how many rings are present.

ii) The term "heterocycle" is indefinite because it is not known how many atoms make up the ring, which atoms are present and what kind of a ring (monocyclic, bicyclic, spiro, fused, bridged, saturated, etc.) is intended.

iii) The last line of the claims reads "and pharmaceutically acceptable salts and individual diastereomers thereof." This is not proper Markush language. It is suggested to use proper alternative language, such as, "or a pharmaceutically acceptable salt or diastereomer thereof." Also, in claim 10, rewriting it in such a way that "and" precedes the last compound is suggested.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim reads on antagonism of

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CGRP receptor activity in a mammal with below normal CGRP activity, antagonism of CGRP receptor activity in a mammal with normal CGRP activity, or in asymptomatic mammals with up-regulated CGRP activity. The specification fails to teach any benefit to be gained from such actions. Is extensive experimentation required on the part of a potential infringer to determine if his use of Applicants' antagonists falls within the limitations of applicants' claim? *In re Kirk and Petrow*, 153 USPQ 48 (CCPA 1967). As the Supreme Court said in *Brenner v. Manson*, 148 USPQ at 696: “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” As U.S. Court of Customs and Patent Appeals stated *In re Diedrich* 138 USPQ at 130, quoting with approval from the decision of the board: “We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would have been obvious to men skilled in the particular art to which this use relates.”

Claim 13 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The how to use requirement of the enablement statute, when applied to method claim, refers to operability and how to make the claimed method work “The factors to be considered (in making an enablement rejection) have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims”, In re Rainer 146 USPQ 218 (1965); In re Colianni, 195 USPQ 150, Ex parte Formal, 230 USPQ 546. The issue is the correlation between clinical efficacy for controlling, ameliorating or preventing migraine headaches or cluster headaches and Applicants' in vitro assays.

a) Determining if any particular claimed compound would treat, control, ameliorate or prevent migraine headaches or cluster headache would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it to clinical trials or testing them in an assay known to be correlated to clinical efficacy of such treatment, control, amelioration or prevention. This is a large degree of experimentation.

b) The direction in the specification merely states Applicants' intention to do so. There are several assays described in the specification with no data. Applicants do not assert and it is not art-recognized that these in vitro assays are correlated to clinical efficacy of the diseases objected to. How is the skilled physician to know what dose to use for each of these different diseases?

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c) There is no working example of treatment, control, amelioration or prevention of migraine headaches or cluster headache in man or animals.

d) The nature of the invention is clinical treatment, control, amelioration or prevention of migraine headaches or cluster headache, which involves physiological activity.

e) The state of the clinical arts in the antagonists of CGRP activity related diseases is extensive with no report of success.

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience.

g) It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved” and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

h) The scope of the claims involves all of the thousands of compounds as well as the treatment of diseases. Thus, the scope of the claim is broad. The scope of uses embraced by these claims is not remotely enabled.

MPEP 2164.01(a) states, “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion is clearly justified here and undue experimentation will be required to practice Applicants' invention.

Deletion of the phrase “controlling, ameliorating or reducing the risk” would overcome this rejection.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruck Kifle whose telephone number is 571-272-0668. The examiner can normally be reached on Mondays-Fridays from 8:30 AM -6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bruck Kifle/
Primary Examiner
Art Unit 1624

BK
March 26, 2008